REMARKS

This is in response to the Official Action mailed December 13, 2002 for the above-captioned patent application. Following the Examiner's restriction requirement, it is understood that Claims 10-11 have been withdrawn from examination. Applicants reserve the right to prosecute Claims 10-11 in a separate patent application. Claims 1-9 and 12-16 are now pending in the above-captioned application. New Claims 12-16 have been added, and Claims 1 and 5-9 have been amended as is further discussed below. New Claims 12-14 depend on Claims 1, 8 and 9, respectively. Each of new Claims 12-14 recites that the compounds formed according to the method claimed in the corresponding independent claim are isolated after formation. It is respectfully submitted that new Claims 12-14 are supported by the specification as originally filed (*see, e.g.,* all examples) and therefore do not constitute new matter. New Claims 15 and 16 depend on Claims 8 and 9, respectively, and further define the reducing agent. It is respectfully submitted that new Claims 15 and 16 are supported by the specification as originally filed (*see, e.g.,* p. 4, line 17-20) and therefore do not constitute new matter. For reasons set forth in detail below, Applicants request that all objections and rejections be withdrawn and that the pending claims be allowed.

The Specification has been amended to recite that this application is a national phase application of International Application No. PCT/EP99/04814, which was filed on July 8, 1999 and which published on January 20, 2000, which in turn claims priority from European Application No. 98112719.4, which was filed on July 9, 1998, and European Application No. 98123949.4, which was filed on December 17, 1998. The Specification has been further amended to correct several errors in the nomenclature of the compounds. The Specification has been further amended throughout to replace the phrase "acyl or acyloxy" with the phrase "acyl, alkoxycarbonyl or aryloxycarbonyl." It is respectfully submitted that the amendment is

supported by the Specification as originally filed (*see* Specification, fourth full paragraph on page 2) and therefore does not constitute new matter.

Non-Art Claim Rejections:

Claims 1-9 have been rejected as allegedly indefinite under 35 U.S.C. § 112, second paragraph. Several grounds have been given for the rejection. Each ground is addressed separately below.

1) Claims 1 and 8-9 have been rejected due to the recitation "in the presence of a nucleophile... and a base." In response, Claims 1 and 8-9 have been amended to replace the recitation "...is converted by means of a hydrolase in the presence of a nucleophile and in the presence of a base" with "treating... with a hydrolase and an effective amount of a nucleophile and a base," in accordance with the Examiner's suggestion. It is respectfully submitted that no new matter has been introduced by the foregoing amendments.

2) Claims 1-9 have been rejected as allegedly failing to particularly point out and distinctly claim the "complete" process of preparing a composition. The Examiner's position is that the complete process includes a recovery or isolation step. In response, Claims 1, 8 and 9 have been amended to replace the recitation "Method for the preparation..." with the recitation "Method for the formation...." It is respectfully submitted that no new matter has been introduced by the foregoing amendments. It is further respectfully submitted that the formation of the compounds recited in Claims 1, 8 and 9 is completely described by the steps recited in the respective claims, and that a separate step of isolation of the compounds formed is not required.

3) The term "general" has been deleted as redundant in all the claims.

4) Claims 8 and 9 have been rejected as allegedly confusing due to the recitation "is reduced." In response, Claims 8 and 9 have been amended to recite that the respective compounds are reduced by treatment with a reducing agent. It is respectfully submitted that the

amendment is supported by the specification as originally filed (*see, e.g.*, p. 4, line 17) and therefore does not constitute new matter.

In view of the foregoing amendments and remarks, withdrawal of the rejection under 35 U.S.C. § 112, second paragraph of Claims 1-9 as indefinite is respectfully requested.

Claims 5-7 have been objected to as being in improper form for not reciting multiple dependencies in the alternative. In response, Claims 5-7 have been amended to depend on Claim 1. In view of the foregoing amendments and remarks, withdrawal of the objection to Claims 5-7 as being in improper form is respectfully requested.

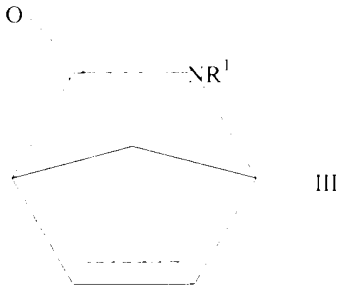
The claims have been further amended throughout to replace the term "acyloxy" with the phrase "alkoxycarbonyl or aryloxycarbonyl." It is respectfully submitted that the amendment is supported by the Specification as originally filed (*see* Specification, fourth full paragraph on page 2) and therefore does not constitute new matter. Claim 9 has been further amended to add asterisks to C-4 and C-1 of formula V. The amendment is supported by Claim 9 as originally filed (*see, e.g.*, formula IV) and therefore does not constitute new matter.

Claim Rejections under 35 U.S.C. §§ 102:

Claims 1-2 and 6-9 have been rejected under 35 U.S.C. § 102(b) as anticipated by "*Biocatalytical Transformations,*" Tetrahedron: Asymmetry, pp. 269-276 (1994) (Csuk et al.). The Examiner alleges that Csuk et al. teach the hydrolysis of 2-azabicyclo[2,2,1]-hept-5-en-3-one using a hydrolase and the subsequent reduction of the product, anticipating the invention claimed in Claims 1-2 and 6-9.

However, it is respectfully submitted that Claims 1-2 and 6-9 are not anticipated by Csuk et al. Anticipation under 35 U.S.C § 102 requires that "all the elements and limitations of the claim be found within a single prior art reference...there must be no difference between the claimed invention and the reference disclosed, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.* 927 F2d 1565, 18

U.S.P.Q. 2d 1001, 18 U.S.P.Q. 2d 1896 (1991). *See also* MPEP 706.02 ("For anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention..."). Claims 1, 8 and 9 as amended expressly recite a compound of formula III:



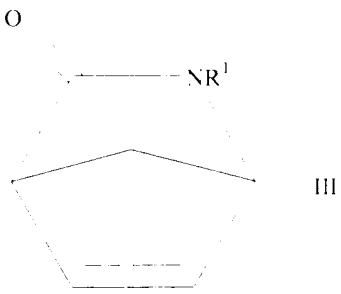
III

wherein R^1 is *acyl, alkoxycarbonyl or aryloxycarbonyl* (emphasis added). In contrast, Csuk et al. only teach the hydrolysis of 2-azabicyclo[2,2,1]-hept-5-en-3-one, which differs from the compound having a formula III in that R^1 is hydrogen (*see* p. 269, second paragraph, third line, and structure (2) on p. 270 of Csuk et al.). Csuk et al. does not disclose the compound of formula III, where R^1 is acyl, alkoxycarbonyl or aryloxycarbonyl, as required by Claims 1, 8 or 9. Accordingly, Csuk et al. does not teach "all the elements and limitations of the claim," as is required for anticipation under 35 U.S.C. § 102. Therefore, it is respectfully submitted that Claims 1, 8 and 9 (and Claims 2 and 6-7 dependent on Claim 1) are not anticipated by Csuk et al.

In view of the foregoing, withdrawal of the rejection under 35 U.S.C. § 102(b) of Claims 1-2 and 6-9 as anticipated by Csuk et al. is respectfully requested.

Claims 1-2 and 6-9 have been rejected under 35 U.S.C. § 102(b) as anticipated by Tetrahedron: Asymmetry, pp. 2382-2386 (1996) (Nakano et al.). The Examiner alleges that Nakano et al. teach the hydrolysis of 2-azabicyclo[2,2,1]-hept-5-en-3-one using a hydrolase and the subsequent reduction of the product, anticipating the invention claimed in Claims 1-2 and 6-9.

However, it is respectfully submitted that Claims 1-2 and 6-9 are not anticipated by Nakano et al. As discussed above, Claims 1, 8 and 9 expressly recite a compound of formula III:



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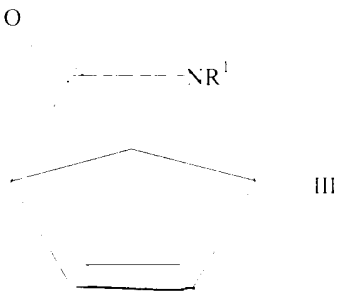
wherein R^1 is *acyl, alkoxycarbonyl or aryloxycarbonyl* (emphasis added). In contrast, Nakano et al. only teach the hydrolysis of 2-azabicyclo[2,2,1]-hept-5-en-3-one, which differs from the compound having a formula III in that R^1 is acetoxymethyl or hydroxymethyl (*see* structures (3) and (4) on pp. 2382-2384 of Nakano et al.). Nakano et al. does not disclose the compound of formula III, where R^1 is acyl, alkoxycarbonyl or aryloxycarbonyl, as required by Claims 1, 8 or 9. Accordingly, Nakano et al. does not teach "all the elements and limitations of the claim," as is required for anticipation under 35 U.S.C. § 102 as discussed above. Therefore, it is respectfully submitted that Claims 1, 8 and 9 (and Claims 2 and 6-7 dependent on Claim 1) are not anticipated by Nakano et al.

In view of the foregoing, withdrawal of the rejection under 35 U.S.C. § 102(b) of Claims 1-2 and 6-9 as anticipated by Nakano et al. is respectfully requested.

Claims 1 and 5-7 have been rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,688,933 (Evans et al.). The Examiner alleges that Evans et al. teach the hydrolysis of 2-azabicyclo[2,2,1]-hept-5-en-3-one using a hydrolase and the subsequent reduction of the product, anticipating the invention claimed in Claims 1 and 5-7.

However, it is respectfully submitted that Claims 1 and 5-7 are not anticipated by Evans et al. As discussed above, Claim expressly recites a compound of formula III:



III

wherein R^1 is *acyl, alkoxycarbonyl or aryloxycarbonyl* (emphasis added). In contrast, Evans et al. only teach the hydrolysis of 2-azabicyclo[2,2,1]-hept-5-en-3-one, which differs from the compound having a formula III in that R^1 is hydrogen (*see* Example 1 and all [2,2,1] bicyclic structures in Evans et al.). Evans et al. does not disclose the compound of formula III, where R^1 is acyl, alkoxycarbonyl or aryloxycarbonyl, as required by Claim 1. Accordingly, Evans et al. does not teach "all the elements and limitations of the claim," as is required for anticipation under 35 U.S.C. § 102 as discussed above. Therefore, it is respectfully submitted that Claims 1 (and Claims 5-7 dependent on Claim 1) is not anticipated by Evans et al.

In view of the foregoing, withdrawal of the rejection under 35 U.S.C. § 102(b) of Claims 1 and 5-7 as anticipated by Evans et al. is respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with Markings to Show Changes Made."**

In view of the foregoing amendments and remarks, reconsideration and allowance of all the claims in this application are respectfully requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

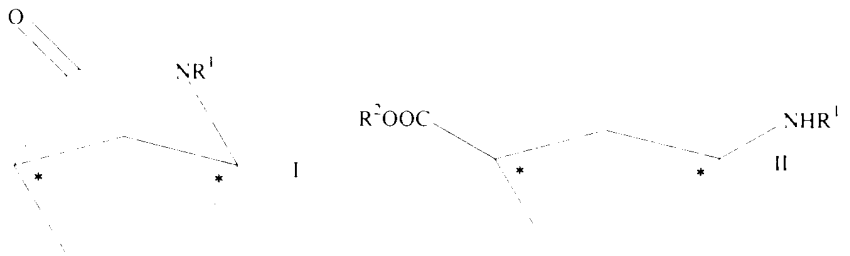
The following paragraph has been inserted on page 1, after the title:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a national phase application of International Application No. PCT/EP99/04814, which was filed on July 8, 1999 and which published on January 20, 2000, which in turn claims priority from European Application No. 98112719.4, which was filed on July 9, 1998, and European Application No. 98123949.4, which was filed on December 17, 1998.

The paragraph beginning on page 1, last line, above formulas I and II, has been amended as follows:

The invention's method for preparing compounds of the general formulas



I II

and

wherein R^1 is acyl [or acyloxy] , alkoxycarbonyl or aryloxycarbonyl and R^2 is a hydrogen atom or C_{1-10} alkyl, [takes place by means of] comprises treating with a hydrolase [in the presence of] and an effective amount of a nucleophile and [in the presence of] a base in a constant pH range [starting with] a racemic lactam of the formula

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The sixth full paragraph on page 2 has been amended as follows:

Hydrolases that can be used are proteases or lipases, preferably proteases, such as [serinproteases] serine proteases. Examples of [serinproteases] serine proteases that can be used are chymotrypsins, trypsins and subtilisins (bacterial [serinproteases] serine proteases). Subtilisins that can be used are commercial subtilisins, such as subtilisin A, subtilisin B, alcalases, ALK enzymes, bacillopeptidase A, bacillopeptidase B, bioprases, colistinases, esperases, genenase I, kazusase, maxacal, maxatases, nagarses, peptidases, protease S, protease VIII, protease XXVII, proteinases, such as the alkaline proteinase of Bacillus subtilis or Aspergillus oryzae, proteinase K from Tritirachium album[in], savinases, subtilopeptidasen, superases, and thermoases. Conducting the biotransformation by means of savinases is preferred. Suitable savinases are savinase 12 Type W™, savinase 16.OL Type EX™, savinase 32.OL Type EX™, savinase 4.OT Type W™, and savinase 8.OL™. The lipase that can be used is, for example, lipase from Candida Antarctica.

The paragraph beginning on page 2, four lines from the bottom, has been amended as follows:

If the hydrolases used are proteases, such as proteases from Bacillus subtilis, proteases from Aspergillus oryzae, proteinase K from Tritirachium album[in], the (1S, 4R) enantiomer in the racemic lactam of formula III is hydrolyzed suitably into the corresponding compound of general formula II, whereby the (1R, 4S) enantiomer of general formula I is obtained. If the hydrolases used are lipases, such as lipase from Candida Antarctica, the (1R, 4S) enantiomer in the racemic lactam of formula III is hydrolyzed suitably into the corresponding compound of general formula II, whereby the (1S, 4R) enantiomer of general formula I is obtained.

The first full paragraph on page 3 has been amended as follows:

[Hydroxide ions, water] Water or C_{1-10} alcohols can be used as the nucleophile. Suitable C_{1-10} alcohols are methanol, ethanol, propanol, isopropanol, butanol, *t*-butanol,

isobutanol, pentanol, hexanol, heptanol, octanol, nonanol or decanol. If the nucleophile used is a C_{1-10} alcohol, the corresponding ester of general formula II ($R^2 = C_{1-10}$ alkyl) is formed, as the expert knows. If water is used as the nucleophile, obviously, the corresponding acid of general formula II ($R^2 = H$) is formed.

The fifth full paragraph on page 3 has been amended as follows:

The biotransformation is suitably conducted in water, a buffer solution, a C_{1-10} alcohol or in a mixture of these with an aprotic organic solvent. Suitable aprotic organic solvents are, for example, ether and aromatic hydrocarbons. Tetrahydrofuran, dioxane or [t-methylbutyl] t-butyl methyl ether can be used as the ether. Toluene and benzene are suitable aromatic hydrocarbons. The buffer solutions used can be, for example, low molarity, such as 10-100 mM sodium or potassium phosphate buffer, hepes buffer. The C_{1-10} alcohols used can be those previously described.

The paragraph beginning on page 3, two lines from the bottom, has been amended as follows:

After a usual conversion time of a few hours depending on the selected starting material, the desired optically active compounds of general formulas I and II are obtained in outstanding yields and enantiomer purity. The preferred starting materials are racemic 2-acetyl-2-azabicyclo-[2.2.1]hept-5-ene-3-one (R^1 = acetyl) and the racemic 2-ethoxycarbonyl-2-azabicyclo-[2.2.1]hept-5-ene-3-one (R^1 = ethoxycarbonyl). The preferred compounds of formula II are (1S, 4R)-[1]4-acetylamino-2-cyclopentene-[4]1-carboxylic acid (R^1 = acetyl, R^2 = H), (1S, 4R)-[1]4-ethoxycarbonylamino-2-cyclopentene-[4]1-carboxylic acid (R^1 = ethoxycarbonyl, R^2 = H), (1S, 4R)-[1]4-acetylamino-2-cyclopentene-[4]1-carboxylic acid methyl ester (R^1 = acetyl, R^2 = CH_3), (1S, 4R)-[1]4-acetylamino-2-cyclopentene-[4]1-carboxylic acid butyl ester (R^1 = acetyl, R^2 = C_4H_9), (1S, 4R)-[1]4-acetylamino-2-cyclopentene-[4]1-carboxylic acid ethyl ester (R^1 = acetyl, R^2 = C_2H_5), and (1S, 4R)-[1]4-acetylamino-2-cyclopentene-[4]1-carboxylic acid propyl ester (R^1 = acetyl, R^2 = C_3H_7). The (1S, 4R)-4-acetylamino-2-cyclopentene-[4]1-carboxylic acid

C_{2-10} alkyl esters, preferably the (1S, 4R)-4-acetylamino-2-cyclopentene-[4]1-carboxylic acid ethyl ester and the (1S, 4R)-4-acetylamino-2-cyclopentene-[4]1-carboxylic acid propyl ester of the formula II are not described in the literature and are similarly part of the invention.

The third full paragraph on page 4 has been amended as follows:

The binary alkali metal borohydrides or alkaline earth metal borohydrides used can be $NaBH_4$, $LiBH_4$, KBH_4, $NaAlH_4$, $LiAlH_4$, $KAlH_4$, $Mg(BH_4)_2$, $Ca(BH_4)_2$, $Mg(AlH_4)_2$, $Ca(AlH_4)_2$. Complex metal hydrides of the boron or aluminum group can have the general formula $M^1M^2H_nL_m$, wherein n is a whole number from 1 to 4, m is a whole number from 4 to [4 minus the corresponding number n] 4-n, M^1 is an alkali metal atom, M^2 is boron or aluminum, and L is C_{1-4} alkyl, C_{1-4} alkenyl, C_{1-4} alkoxy, CN or an amine, or the complex metal hydrides can have the general formula $M^2H_OL_p$, wherein M^2 is as already named, [O]o is a whole number from 0 to 3, and p is a whole number from 3 to [3 minus the corresponding number p] 3-o. The $M^1M^2H_nL_m$ used can be $LiBH(C_2H_5)_3$, $LiBH_x(OCH_3)_{[4-1]4-x}$, wherein x is a whole number from 1 to 3, $LiAlH(OC(CH_3)_3)_3$, $NaAlH_2(OC_2H_4OCH_3)_2$, $NaAlH_2(C_2H_5)_2$ or $NaBH_3CN$. The reduction is conducted preferably with a metal borohydride, such as sodium borohydride.

The fourth full paragraph on page 10 has been amended as follows:

1.3 Reduction of (1R,4S)-2-acetyl-2-azabicyclo[2.2.1]hept-5-ene-3-one to (1R,4S)-[2]1-acetyl[-1-]amino-4-(hydroxymethyl)-2-cyclopentene.

The paragraph beginning on page 10, six lines from the bottom has been amended as follows:

287.4 g (-)-acetyl-2-azabicyclo[2.2.1]hept-5-ene-3-one (100% ==> ~255 ml, 97%; 1.9 moles) were dissolved in 380 ml water and 1217 ml 2-butanol. The solution was cooled to 0 to -2 °C. 45 g $NaBH_4$ (1.188 moles, 1.25 eq.) were suspended in 304 ml fresh 2-butanol in another stirring device. The $NaBH_4$ suspension was added to the solution during 1- 2 hours. The reaction was exothermic, and the temperature was not allowed to exceed 5 °C. The temperature had to be at 0° C before a portion was added. The reaction was followed by DC (thin-layer

chromatography) (hexane/etrol/MeOH: 5/5/1). The reaction was allowed to continue for 1 to 2 hours after the addition. When the reaction was complete (educt concentration had to be at < 1.0 %), the pH was adjusted to 2 with ca. 135 g concentrated hydrochloric acid. The temperature was maintained below 10°C. The pH was then adjusted immediately to 9 with ca. 85 ml 30% sodium hydroxide solution. The precipitated salts were filtered and washed with 127 ml fresh 2-butanol. The filtrate and the "2-butanol wash" were combined, and the phases separated. The aqueous phase was extracted twice with 380 ml fresh 2-butanol each time. The 2-butanol phases were combined. Ca. 2450 g of a 10% solution of the product, (1R,4S)-[2]1-acetyl[-1-]amino-4-(hydroxymethyl)-2-cyclopentene, were obtained in 2-butanol. This corresponded to ca. 250 g of 100% product, (1R,4S)-[2]1-acetyl[-1-]amino-4-(hydroxymethyl)-2-cyclopentene, corresponding to a yield of 85%.

The first full paragraph on page 11 has been amended as follows:

1.4 Hydrolysis of (1R,4S)-[2]1-acetyl[-1-]amino-4-(hydroxymethyl)-2-cyclopentene to (1R,4S)-1-amino-4-(hydroxymethyl)-2-cyclopentene.

The second full paragraph on page 11 has been amended as follows:

1.4.1 30% NaOH (45 g) was added to 49.3 g (0.28 mole) (1R, 4S)-[2]1-acetyl[-1-]amino-4-(hydroxymethyl)-2-cyclopentene, and the suspension was heated to 100 °C. After 3.5 hours, the solution was cooled to 0°C and then adjusted to pH = 1.0 with concentrated HCl. Water was evaporated and NaCl filtered off. Pentanol (2 ml per go of residue) and acetone (6 ml per gram of residue) were added. The resulting precipitate was filtered and washed with 20 ml acetone. 37.5 g (0.24 mole) of product were obtained as the hydrochloride salt having an ee = 99%, corresponding to a yield of 86%.

The third full paragraph on page 11 has been amended as follows:

1.4.2 85.4 g [(-)-2](1R,4S)-(-)-1-acetyl[-1-]amino-4-(hydroxymethyl)-2-cyclopentene 100% (0.55 mole) was prepared as a 10% solution in 2-butanol. It was distilled

until the distillate ceased. Then 100.0 g of a 30% sodium hydroxide solution (==> 33.0 g NaOH 100%; 0.825 mole, 1.5 eq) and 65 g water were added. The remaining 2-butanol was removed (with ca.l 10 g water) by azeotropic distillation. The solution was heated at reflux (100 – 100° C) for 4-5 hours. The reaction was followed by GC. When the conversion was complete, the reaction was cooled to 50° C, and 154 ml 2-butanol (124.3 g) were added. The phases were separated at 50 °C 915 minutes stirring, phases separate). The aqueous phase (ca. 165 g) was discarded. The organic phasese were combined, and ca. 22 g hydrogen chloride were added at 20 – 40 °C to make pH 1. Some salts precipitated during the acidification. These salts were filtered off at 20°C, and the filtrate was distilled under standard pressure until 220 ml distillate (ca. 180 g) were collected (boiling temperature ca. 91- 92 °C). At ca. 70° C, 176 ml acetone (139.0 g) were added. The suspension was stirred at reflux for 15-30 minutes and then cooled to –5°C. After 1 hour at this temperature was filtered off by suction, and the filter cake was washed with 154 ml acetone. 70 g of (-) of 100 % product were obtained, corresponding to a yield of 85%.

The third full paragraph on page 12 has been amended as follows:

109.13 g racemic 2-[ethoxycarbonyl-2-]azabicyclo[2.2.1]hept-5-ene-3-one were mixed with 182.1 g triethylamine, 6.11 g 4-dimethylaminopyridine and 500 ml acetonitrile. The reaction was heated to 50° C. Then, 195.3 g ethyl chloroformate, dissolved in 150 ml acetonitrile, were added portionwise. The temperature was maintained below 55° C. After the reaction ended, the solution was cooled to 20° C. The salts were filtered off and washed with acetonitrile. The filtrate was concentrated at 60° C and 20 mbar, and then mixed with 1500 ml toluene. Three extractions followed: with 250 ml water, pH 8, with 250 ml acetic acid (1%) and with 250 ml saturated NaCl solution. The organic phase was dried with $MgSO_4$ and concentrated at 80° C 20 mbar. 167.4 g of a brown oil were obtained. The content by GC was

96% (±)-2-ethoxycarbonyl-2-azabicyclo[2.2.1]hept-5-ene-3-one, which was purified by vacuum distillation, $b.p._{0.01} = 76.5\ ^{o}C$, content (GC): 99.5%, yield: 156.6 g (88.5%).

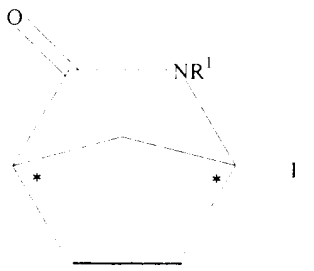
The fifth full paragraph on page 12 has been amended as follows:

The product was prepared as in Example 2.1, starting from [(-)-2-ethoxycarbonyl-](1R,4S)-(-)-2-azabicyclo[2.2.1]hept-5-ene-3-one.

In the Claims:

Claims 1 and 5-9 have been amended as follows:

1. (Amended) Method for [preparing] forming optically active compounds of the [general] formula[s]e



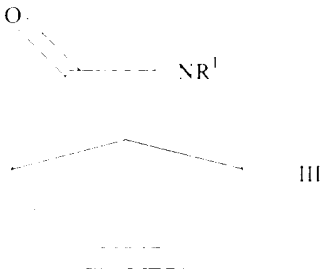
I

II

and

wherein R^1 is acyl [or acyloxy] , alkoxycarbonyl or aryloxycarbonyl and R^2 is a hydrogen atom or C_{1-10} alkyl,

[wherein] the method comprising treating a racemic lactam of the [general] formula



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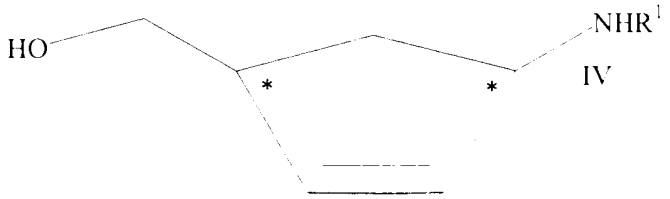
[is converted by means of] with a hydrolase [in the presence of] and an effective amount of a nucleophile and [in the presence of] a base in a constant pH range to form the optically active compounds of formulae I and II.

5. (Amended) Method according to [at least one of Claims 1 to 4] Claim 1, [characterized in that] wherein 2-acetyl-2-azabicyclo[2.2.1]hept-5-ene-3-one or 2-ethoxycarbonyl-2-azabicyclo[2.2.1]hept-5-ene-3-one is used as the racemic lactam of [general] formula III.

6. (Amended) Method according to [at least one of Claims 1 to 5] Claim 1, [characterized in that] wherein the [conversion] treatment of the racemic lactam is conducted in water, a buffer solution, a C_{1-10} alcohol or in a mixture of these with an aprotic solvent.

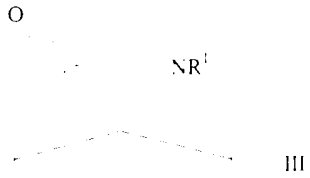
7. (Amended) Method according to [at least one of Claims 1 to 6] Claim 1, [characterized in that] wherein the [reaction] treatment of the racemic lactam is conducted at a temperature of 10 to 60 °C.

8. (Amended) Method for the [preparation] formation of optically active 1-amino-4-(hydroxymethyl)-2-cyclopentene derivatives of the [general] formula



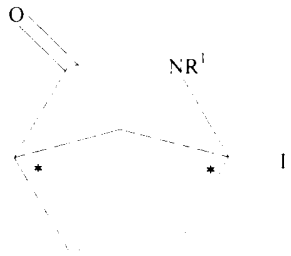
IV

wherein R^1 is [the same as in Claim 1] acyl, alkoxycarbonyl or aryloxycarbonyl , [characterized in that] the method comprising treating a lactam of the [general] formula



III

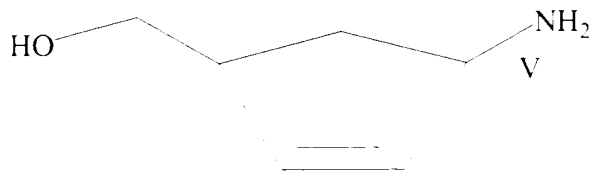
wherein R^1 is [the same as in Claim 1] acyl, alkoxycarbonyl or aryloxycarbonyl [is converted by means of] with a hydrolase [in the presence of] and an effective amount of a nucleophile and [in the presence of] a base in a constant pH range [into] to form the compound of the [general] formula

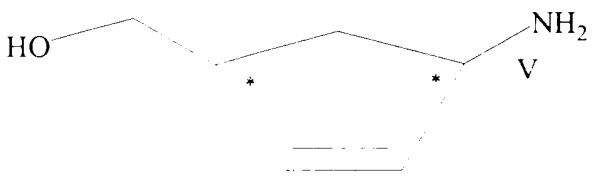


I

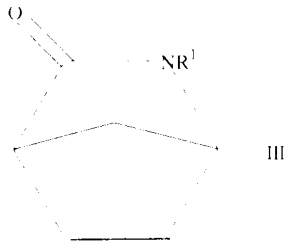
and [this] wherein the compound of the formula I is reduced to the compound of [general] formula IV by treatment with a reducing agent.

9. (Amended) Method for the [preparation] formation of (1R, 4S)-1-amino-4-(hydroxymethyl)-2-cyclopentene of the formula

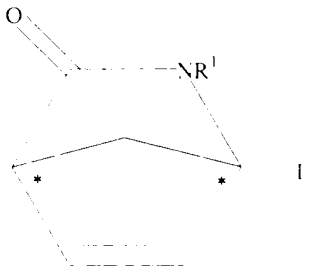




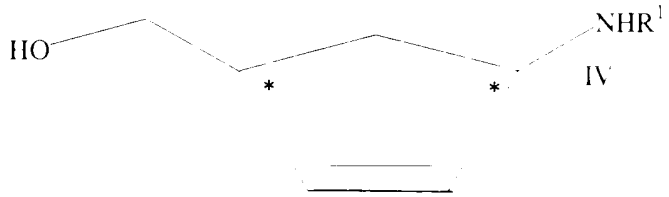
or its salts, [characterized in that] the method comprising treating a lactam of the [general] formula



wherein R^1 is [the same as in Claim 1] acyl, alkoxycarbonyl or aryloxycarbonyl [is converted by means of] with a hydrolase [in the presence of] and an effective amount of a nucleophile and [in the presence of] a base in a constant pH range [into] to form the compound of the [general] formula



wherein R^1 is [the same as in Claim 1] acyl, alkoxycarbonyl or aryloxycarbonyl, [this] wherein the compound of the formula I is then reduced to the compound of [general] formula



by treatment with a reducing agent, wherein R^1 is [the same] acyl, alkoxycarbonyl or aryloxycarbonyl, and [this] wherein the compound of the formula IV is then hydrolyzed to the compound of [general] formula V.

The following new claims have been added:

12. (New) The method of Claim 1, wherein each of the optically active compounds of formulae I and II is isolated after formation.

13. (New) The method of Claim 8, wherein the optically active 1-amino-4-(hydroxymethyl)-2-cyclopentene derivatives of the formula IV are isolated after formation.

14. (New) The method of Claim 9, wherein the (1R, 4S)-1-amino-4-(hydroxymethyl)-2-cyclopentene of the formula V is isolated after formation.

15. (New) The method of Claim 8, wherein the reducing agent is a metal hydride.

16. (New) The method of Claim 9, wherein the reducing agent is a metal hydride.